

**TITLE**

Corticospinal excitability during shortening and lengthening actions with incremental torque output

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Škarabot, Jakob; Tallent, Jamie; Goodall, Stuart; et al.

**JOURNAL**

Experimental physiology

**DATE DEPOSITED**

3 October 2018

**This version available at**

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1 **CORTICOSPINAL EXCITABILITY DURING SHORTENING AND LENGTHENING**  
2 **ACTIONS WITH INCREMENTAL TORQUE OUTPUT**

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9

10 **Running title:** Evoked potentials during lengthening actions of increasing strength

11 **Key words:** eccentric contractions, electromyography, transcranial magnetic stimulation

12 **Word count (with references):** 3944

13 **References:** 41

14

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25 **What is the central question of this study?**

26 Relationship between motor unit recruitment and firing rate has been related to the size of the  
27 corticospinal output with variations in the nervous system gain during isometric contractions.  
28 However, corticospinal behaviour with incremental torque output might differ during  
29 anisometric contractions due to differences in neural control of anisometric contraction types.

30 **What is the main finding and its importance?**

31 Corticospinal excitability during lengthening contractions was smaller compared to  
32 shortening, but increased with incremental torque output similarly between contraction types.  
33 This suggests that the relationship between motor unit recruitment and firing rates is the likely  
34 main determinant of the size of an evoked response with variations in system gain.

35

36

**ABSTRACT**

37 The modulation of motor evoked potentials (MEPs), an index of corticospinal excitability, has  
38 been shown to increase during isometric contractions with incremental torque output in  
39 accordance with the contribution between motor unit recruitment and firing rate of the muscle  
40 to increases in required torque output. However, motor unit strategy of the muscle might not  
41 be the only factor influencing this behaviour since differences in pre- and postsynaptic control  
42 have been reported between lengthening and shortening or isometric contractions. In thirty  
43 healthy adults, MEPs were elicited in tibialis anterior during shortening and lengthening  
44 contractions at 15, 25, 50 and 80% contraction type specific maximal voluntary contraction  
45 torque. Background electromyographic activity increased progressively with greater torque  
46 output ( $p < 0.001$ ), but was similar between contraction types ( $p = 0.162$ ). When normalised to  
47 the maximal muscle response, MEPs were greater during shortening compared to lengthening

48 contractions ( $p=0.004$ ) and increased step-wise with increased contraction intensities  
49 ( $p=0.001$ ). These data show an increase in corticospinal excitability with torque output from  
50 lower to higher contraction intensities, suggesting greater contribution of motor unit  
51 recruitment to increased nervous system gain in the tibialis anterior. Despite differences in  
52 corticospinal control of shortening and lengthening contractions, the data suggest the  
53 corticospinal responses to increases in torque output are not dependent on contraction type  
54 since corticospinal excitability increased similarly during shortening and lengthening actions.  
55 Thus, it is likely that the relationship between motor unit recruitment and firing rate of the  
56 muscle is the main determinant of corticospinal output with variations in nervous system gain.

## INTRODUCTION

57

58 The size of the motor evoked potentials (MEPs) when normalised to a maximal muscle  
59 response, an index of corticospinal excitability, is modulated by varying the nervous system  
60 gain. Data from isometric experimental models suggests that an increase in contraction  
61 strength or voluntary drive results in increased MEP size (peak to peak amplitude or area),  
62 sometimes followed by a decline, or plateau, at higher contraction strengths depending on the  
63 muscle (Goodall, Romer, & Ross, 2009; Martin, Gandevia, & Taylor, 2006; Todd, Taylor, &  
64 Gandevia, 2003; Weavil, Sidhu, Mangum, Richardson, & Amann, 2015). Specifically,  
65 muscles which rely on a greater degree of motor unit recruitment in response to an  
66 incremental force increase are likely to exhibit a peak in the evoked response at higher  
67 percentage of maximal contraction strength (Gelli, Del Santo, Popa, Mazzocchio, & Rossi,  
68 2007; Martin et al., 2006). On the other hand, muscles that rely more on increases in motor  
69 unit firing rate for increases in force production are likely to exhibit a plateau or a decline in  
70 corticospinal excitability at lower percentages of maximal strength. This is due to the negative  
71 correlation between increases in motor unit firing rate and the probability of an evoked  
72 response (Bawa & Lemon, 1993; Brouwer, Ashby, & Midroni, 1989; Jones & Bawa, 1999).  
73 For example, the majority of arm and hand muscles (Todd *et al.*, 2003; Martin *et al.*, 2006) as  
74 well as the quadriceps (Goodall et al., 2009; Weavil et al., 2015) exhibit a peak in evoked  
75 response size followed by a decline at contraction strengths  $\geq 50-75\%$  of maximal voluntary  
76 contraction (MVC) during isometric conditions. However, the triceps brachii (Todd et al.,  
77 2003) and some lower limb muscles, such as the soleus, exhibit a continuous increase in MEP  
78 size with force output (Oya, Hoffman, & Cresswell, 2008), consistent with the relationship  
79 between motor unit recruitment and firing rates in a muscle.

80 The motor unit strategy of a muscle might not be the only factor determining the corticospinal  
81 output with increases in nervous system gain. For example, corticospinal excitability has been

82 shown to be reduced during maximal (Doguet et al., 2017; Julien Duclay, Pasquet, Martin, &  
83 Duchateau, 2011) and submaximal (Abbruzzese, Morena, Spadavecchia, & Schieppati, 1994;  
84 J. Duclay, Pasquet, Martin, & Duchateau, 2014; Gruber, Linnamo, Strojnik, Rantalainen, &  
85 Avela, 2009) lengthening compared to shortening and/or isometric contractions at a similar  
86 relative torque output. Some researchers have made inferences that the corticospinal  
87 behaviour might be similar during shortening and lengthening contractions with increases in  
88 torque output (J. Duclay et al., 2014), but these investigations have been limited in the number  
89 of contraction intensities studied. Thus, it remains contentious whether a similar trend of the  
90 contraction intensity–MEP response curve is observed during the two types of anisometric  
91 contraction. Therefore, the purpose of this study was to assess the effect of contraction  
92 intensity during shortening and lengthening contractions on the modulation of MEP  
93 amplitude. Only submaximal intensities up to 80% MVC were studied since they have a  
94 greater relevance to the activities of daily living and in order not to confound the corticospinal  
95 behaviour in the present study with potential fatigue. We hypothesised that MEPs would be  
96 lower during lengthening compared to shortening contractions, but, based on previous work in  
97 the soleus, the contraction intensity-MEP curves would exhibit similar profiles during both  
98 contractions types. The tibialis anterior (TA) was chosen as the muscle of interest due to its  
99 unique characteristics. Specifically, dorsiflexors have been shown to exhibit greater torque  
100 producing capacity during lengthening compared to shortening contraction (Pasquet *et al.*,  
101 2000; Reeves & Narici, 2003; Klass *et al.*, 2007; Duchateau & Enoka, 2016), which might not  
102 be the case for all human muscles (Duchateau & Enoka, 2016). Furthermore, due to its role in  
103 locomotion (Byrne, O’Keeffe, Donnelly, & Lyons, 2007) and the need for accuracy of toe  
104 clearance (Capaday, Lavoie, Barbeau, Schneider, & Bonnard, 1999), the TA exhibits a  
105 facilitated corticospinal response during human walking (Capaday et al., 1999; Schubert,

106 Curt, Jensen, & Dietz, 1997) highlighting the functional need to investigate the corticospinal  
107 behaviour of this specific muscle.

108

## 109 **METHODS**

### 110 **Ethical approval**

111 The procedures of this study were approved by Northumbria University Faculty of Health &  
112 Life Sciences Ethics Committee (RE070112538) in accordance with Declaration of Helsinki  
113 with the exception of registration in a database.

114

### 115 **Participants**

116 Thirty healthy, young individuals (including 6 females;  $25 \pm 4$  yrs;  $175 \pm 10$  cm,  $76.1 \pm 9.9$   
117 kg) provided written informed consent to take part in the study. Participants were both from  
118 resistance-trained ( $n = 4$ ) and untrained population since previous work has shown no effect  
119 of resistance-training status on MEP amplitude in the TA (Tallent, Goodall, Hortobágyi, St  
120 Clair Gibson, & Howatson, 2013). A mixed-sex sample was studied to be able to extrapolate  
121 the findings to a wider population. However, as highlighted recently (Sims & Heather, 2018),  
122 controlling for changes in hormonal milieu is necessary for human physiological studies  
123 including both sexes. To reduce the potential influence of female sex hormones on neuronal  
124 function (Smith, Adams, Schmidt, Rubinow, & Wassermann, 2002), all females were tested  
125 in the early follicular phase of the menstrual cycle where the quantities of both oestrogen and  
126 progesterone are likely to be low (Elliott, Cable, Reilly, & Diver, 2003). The start of the early  
127 follicular phase was defined as the onset of menstruation and participants were tested within 3  
128 days of that. All participants were free of cardiorespiratory, neurological, neuromuscular

129 disorders or lower body musculoskeletal injury. They also reported no contraindications to  
130 transcranial magnetic stimulation (TMS) and were not taking any medication known to affect  
131 the nervous system. Participants refrained from caffeine and strenuous exercise for 6 and 48  
132 hours prior to the experimental session, respectively.

133

## 134 **Study design**

135 Participants visited the laboratory twice, first for familiarisation followed by the experimental  
136 session 48-72 hours after. The familiarisation session included habituation with stimulation  
137 techniques and practice of the torque-matching task during different contraction types and  
138 intensities as per the experimental protocol which was performed in its entirety. During the  
139 experimental session, participants had MEPs elicited during shortening and lengthening  
140 contractions in the TA across a range of contraction intensities (15, 25, 50 and 80% of  
141 contraction type specific MVC). The order of contraction type and intensity were randomised.  
142 Eight trials were performed per contraction type and intensity and those responses were  
143 averaged and used for data analysis. The experimental protocol is depicted in Figure 1.

144

## 145 **Procedures**

### 146 *Experimental setup*

147 Participants were sat in an isokinetic dynamometer (Cybex Norm, NY, USA) with the foot of  
148 the dominant limb strapped firmly on the motor plate of the device with the knee and hip kept  
149 at 120° (180° = full extension) and 90°, respectively. Contractions were performed by  
150 assisting or resisting the power head of the device during shortening and lengthening actions,  
151 respectively, as the ankle moved through a 30° range of motion (75° to 105°) at an angular



152 velocity of  $15^{\circ}\cdot\text{s}^{-1}$ . All stimuli were applied as the ankle passed through anatomical zero  
153 ( $90^{\circ}$ ). Prior to eliciting MEPs during shortening and lengthening dorsiflexion, a specific  
154 contraction type MVC was performed (Škarabot et al., 2018), with the MVC torque value  
155 recorded at anatomical zero.

156

### 157 *Electromyography*

158 Surface electromyography (EMG) was recorded using bipolar EMG electrodes (8 mm  
159 diameter, 20 mm inter-electrode distance; Kendall 1041PTS, Tyco Healthcare Group, MA,  
160 USA) placed on the belly of TA at one-third of the length between the head of the fibula and  
161 the medial malleolus with the reference electrode on the medial malleolus according to  
162 SENIAM recommendations (Hermens, Freriks, Disselhorst-Klug, & Rau, 2000). Prior to  
163 placement of electrodes, the recording site was shaved, abraded with preparation gel and  
164 wiped clean with an alcohol swab to ensure appropriate impedance ( $< 2 \text{ k}\Omega$ ). The EMG signal  
165 was amplified ( $\times 1000$ ), band pass filtered (10-1000 Hz; D360, Digitimer, Hertfordshire, UK)  
166 and sampled at 5 kHz (CED Power 1401, Cambridge Electronic Design, UK).

167

### 168 *Transcranial magnetic stimulation*

169 A magnetic stimulator (Magstim 200<sup>2</sup>, Magstim Ltd., UK; maximal output of  $\sim 1.4 \text{ T}$ ) with a  
170 posterior-to-anterior current, 110 mm double-cone coil was used to evoke MEPs in TA of the  
171 dominant leg. Initially, the coil was positioned over the reported optimal spot for stimulation  
172 of the TA muscle, roughly 0.5-1 cm lateral and posterior to the vertex (Devanne, Lavoie, &  
173 Capaday, 1997), after which the coil was moved around the initial spot in small steps until the  
174 position evoking the biggest potential in TA (hotspot) was found. After that, resting motor

175 threshold (RMT) was determined, defined as a stimulus intensity that evoked peak-to-peak  
176 MEP amplitude  $\geq 50 \mu\text{V}$  in 5 out of 10 trials (Rossini et al., 2015). During the experiment, the  
177 pulses were delivered at  $1.2 \times \text{RMT}$  as it lies on the middle portion of the ascending part of  
178 the stimulus-response curve (Han, Kim, & Lim, 2001) and is thus sensitive to changes in  
179 corticospinal excitability. All contractions were separated at least 30 seconds to ensure MEPs  
180 had returned to resting values (Tallent et al., 2012).

181

### 182 *Percutaneous nerve stimulation*

183 The maximal muscle response ( $M_{\text{max}}$ ) was elicited with a 40 mm diameter cathode/anode  
184 arrangement over the peroneal nerve (1 ms pulse duration; Digitimer DS7AH, Welwyn  
185 Garden City, Hertfordshire, UK). Once optimal electrode location had been identified, it was  
186 marked with a permanent marker and the electrode was strapped to participant's leg. The  
187 current of the stimulation was increased until no further increase in the evoked response  
188 during rest was observed, after which the current was additionally increased by 50% to ensure  
189 supramaximal intensity of stimulation. To account for possibility of  $M_{\text{max}}$  modulation with  
190 contraction type and intensity (Lee & Carroll, 2005),  $M_{\text{max}}$  was then elicited during specific  
191 muscle action (shortening and lengthening) and intensity (15, 25, 50 and 80% of contraction  
192 type specific MVC) and later used to normalise responses to TMS.

193

### 194 **Data analysis**

195 All data were recorded in a 500 ms window including 50 ms before TMS was delivered  
196 (Signal v3, CED, UK). Background EMG activity was assessed as the mean rectified EMG  
197 activity obtained 25 ms prior to the stimulus and was normalised to peak-to-peak amplitude of

198  $M_{\max}$  (EMG/ $M_{\max}$ ; Lanza *et al.*, 2018). Peak-to-peak amplitude of MEP was calculated and  
199 expressed relative to the amplitude of  $M_{\max}$  (MEP/ $M_{\max}$ ).

200

## 201 **Statistical analysis**

202 A  $2 \times 4$  ANOVA (2 – contraction type, 4 – contraction intensity) was performed to assess the  
203 effect of contraction type and intensity on EMG/ $M_{\max}$  and MEP/ $M_{\max}$  (SPSS Inc., Chicago,  
204 IL, USA). Post hoc analyses were performed using pairwise comparison with Bonferroni  
205 correction. Significance was accepted at an alpha level of 0.05. All data are presented as  
206 means  $\pm$  standard deviation (SD).

207

208

## **RESULTS**

209 EMG/ $M_{\max}$  increased with contraction intensity ( $F_{1.2, 33.4} = 101.8$ ,  $p < 0.001$ ,  $\eta_p^2 = 0.78$ ) in a  
210 progressive manner ( $p < 0.001$  for all; Figure 2A), but was similar between contraction types  
211 ( $F_{1, 29} = 2.0$ ,  $p = 0.171$ ,  $\eta_p^2 = 0.06$ ). However, MEP/ $M_{\max}$  was greater during shortening  
212 compared to lengthening contractions ( $F_{1, 29} = 13.6$ ,  $p = 0.001$ ,  $\eta_p^2 = 0.32$ ), but also increased  
213 with contraction intensity ( $F_{1.6, 46.6} = 86.6$ ,  $p < 0.001$ ,  $\eta_p^2 = 0.75$ ) in a step-wise manner ( $p <$   
214  $0.001$  for all; Figure 2B) during both contraction types.

215 The continual increase in corticospinal excitability across contraction intensities is also shown  
216 in a representative example (Figure 3). MEP/ $M_{\max}$  ratio in this participant increased from 0.38  
217 to 0.42, 0.46 and 0.56 during shortening and from 0.30 to 0.38, 0.40 and 0.50 during  
218 lengthening contractions at 15, 25, 50 and 80% MVC. The behaviour was similar across all  
219 participants (Figure 4).

220

221

## DISCUSSION

222 The present data showed an increase in the size of the MEP amplitude with incremental  
223 torque output up to 80% of maximal torque regardless of contraction type. This is the first  
224 study to have explored the behaviour of corticospinal excitability with varying nervous  
225 system gain and corroborates the experiments using isometric experimental models on other  
226 lower leg muscles such as gastrocnemius and soleus where continual increase in corticospinal  
227 and spinal excitability was observed with increments in torque output (Oya et al., 2008). This  
228 has been related to the motor unit recruitment being the primary strategy for incremental force  
229 control in plantarflexors (Grillner & Udo, 1971). However, the opposite is seen in muscles  
230 such as brachioradialis where increases in firing rate largely contribute to increments in force  
231 production at forces  $\geq 75\%$  MVC, resulting in a decrease in corticospinal excitability at high  
232 contraction strengths (Martin et al., 2006). Specifically, this decrease in corticospinal  
233 excitability has been related to unresponsiveness of the motoneuron pool to an external  
234 stimulus, which is likely due to refractory motoneurons as part of the after-hyperpolarisation  
235 of an action potential (Martin et al., 2006). As evidenced by animal work (Baldissera &  
236 Gustafsson, 1974; Schwindt & Calvin, 1972) and modelling studies (Jones & Bawa, 1999;  
237 Matthews, 1999), motoneurons exhibit an exponential return to threshold when firing rates are  
238 lower, whereas a more progressive return is evident with a greater discharge rate. Data from  
239 single motor unit recordings suggests that during non-ballistic contractions the TA exhibits a  
240 progressive recruitment of motor units up to  $\sim 90\%$  MVC (Desmedt & Godaux, 1977; Van  
241 Cutsem, Duchateau, & Hainaut, 1998). Thus, given motor unit recruitment is the primary  
242 strategy of the TA for increasing force output, the graded increase in corticospinal excitability  
243 across contraction intensities in the present study supports the notion that the behaviour of  
244 evoked potentials is related to the motor unit strategy of a muscle.

245 Another factor that can affect the behaviour of corticospinal excitability with variations in  
246 torque output is the TMS stimulus intensity. It has been shown in upper limb muscles, with  
247 lower a stimulus intensity, a peak in MEP, followed by a MEP decline, occurs at a greater  
248 percentage of MVC compared to higher stimulus intensities (Martin et al., 2006). However, in  
249 lower limb muscles with smaller firing frequency of motor units, the decline in MEP at higher  
250 contraction intensity was not observed with higher stimulus intensity; rather the responses  
251 only plateaued (Oya et al., 2008). We did not examine the responses at intensities  
252 corresponding to maximal MEP amplitude and thus this question could be an avenue worth  
253 exploring in future investigations since it remains possible that different results would be  
254 obtained in the present study had greater TMS stimulus intensity been used. Furthermore, it  
255 has been suggested that the weaker projections to lower limb muscles might be responsible  
256 for the continual increase in corticospinal excitability with increased contraction strengths  
257 (Oya et al., 2008). However, the present data in the TA, a muscle which has a preferential  
258 input from the pyramidal tract into the spinal networks (Brooks & Stoney, 1971), and similar  
259 strength of corticomotoneuronal projections to the upper limbs (Brouwer & Ashby, 1990),  
260 suggest this is not the case. Therefore, it appears that motor unit control is still the primary  
261 factor determining a corticospinal response as the contraction intensity increases.

262 The continual increase of corticospinal output was observed during both shortening and  
263 lengthening contractions, despite a reduced corticospinal excitability during lengthening  
264 relative to shortening contractions, in line with other muscles of the upper and lower limbs (J.  
265 Duclay et al., 2014; Gruber et al., 2009). A previous study has shown a continual increase in  
266 corticospinal excitability from submaximal to maximal contraction strength in the soleus (J.  
267 Duclay et al., 2014), but the study was limited in the contraction strengths studied (only 50%  
268 and 100% MVC). Accordingly, the present study extends this observation of corticospinal  
269 excitability modulation with variations in torque output regardless of contraction type, across

270 differing submaximal intensities. Unlike the soleus, the difference in corticospinal output  
271 between shortening and lengthening contractions in medial gastrocnemius during submaximal  
272 contractions was absent during an MVC (J. Duclay et al., 2014). Since the present study did  
273 not investigate corticospinal excitability during maximal shortening and lengthening actions  
274 due to their lack of relevance in functional activities of daily living, it remains unknown  
275 whether similar behaviour is evident in TA. Thus, it is important to consider the responses  
276 observed in the present study in the context of the muscle and contraction intensities  
277 investigated. Whilst maximal contraction intensities are rarely going to be relevant for  
278 activities of daily living, inclusion of responses to TMS during maximal contractions, that  
279 represent the limit of torque producing capacity of an individual, and muscles with different  
280 motor unit recruitment strategies (e.g. the TA versus a hand muscle) would provide a more  
281 complete picture of corticospinal behaviour during different muscle actions with incremental  
282 torque output and might be something worth exploring in future studies. Given the reported  
283 motor unit control strategy of the TA with incremental torque output, it could be hypothesised  
284 that the evoked responses would peak at ~90% MVC (Desmedt & Godaux, 1977; Van  
285 Cutsem et al., 1998).

286 In conclusion, the contraction type–response curve of MEPs is similar during shortening and  
287 lengthening contractions when normalised to a contraction specific MVC. Despite differences  
288 in neural control of shortening and lengthening contractions, it appears that the relationship  
289 between motor unit recruitment and firing rate is the main mechanism determining  
290 corticospinal output with variations in nervous system gain.

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432

433 **Competing interests**

434 The authors have no competing interests to declare, financial or otherwise.

435

436 **Funding**

437 No funding was received for this study.

438

439 **Acknowledgements**

440 The authors are grateful to Mr. Paul Ansdell for information regarding neurophysiological  
441 testing in female and mixed-sex populations.

442

443 **Author Contributions**

444 Experiments were performed in the Biomechanics Laboratory at Northumbria University. JŠ,  
445 JT, SG and GH designed the study protocol; JT acquired the data; JŠ, JT, SG, RD and GH  
446 analysed and interpreted the data; JŠ, JT, SG, RD and GH drafted or revised the final  
447 manuscript. All authors approved the final version of the manuscript and agree to be  
448 accountable for all aspects of the work. All persons listed qualify for authorship.

449 **Figure captions**

450 Figure 1. The experimental protocol. Participants first performed maximal shortening and  
451 lengthening contractions (MVC; randomised order) which was subsequently used for  
452 calculation of submaximal contraction intensities. Thereafter, participants performed  
453 shortening and lengthening contractions at 15, 25, 50 and 80% of contraction type  
454 specific MVC (pseudorandomised order) whilst receiving transcranial magnetic  
455 stimulation (black downward arrow) and percutaneous stimulation over the peroneal  
456 nerve (grey downward arrow) to elicit motor evoked potentials (MEP) and maximal  
457 compound action potentials ( $M_{\max}$ ), respectively. Participants performed the same  
458 protocol 2-3 days prior to the experimental session for the purposes of familiarisation.

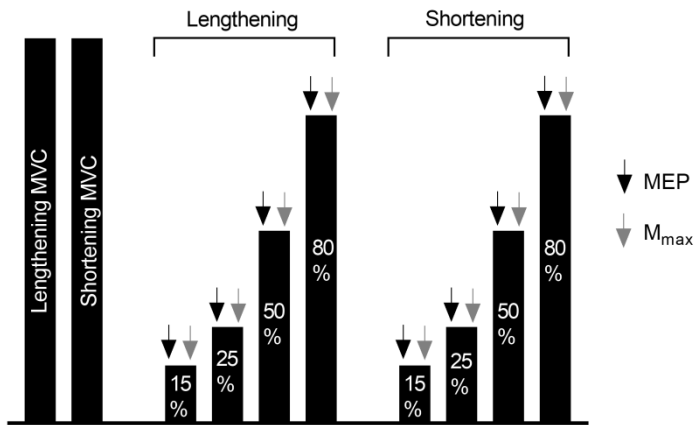
459 Figure 2. Grouped data (mean  $\pm$  SD) for background EMG activity ( $EMG/M_{\max}$ ; A) and  
460 motor evoked potentials normalised to maximal muscle response ( $MEP/M_{\max}$ ; B) during  
461 shortening and lengthening contractions at 15, 25, 50 and 80% of contraction-type  
462 specific maximal torque. \* $p < 0.005$  relative to lengthening, # $p < 0.001$  relative to other  
463 contraction strengths.

464 Figure 3. A representative example of motor evoked potentials across contraction intensities  
465 (15, 25, 50 and 80% MVC torque) during shortening (A) and lengthening (B)  
466 contractions from an individual that best represents the sample mean. Responses are  
467 shown from 50 ms before to 250 ms after the stimulus (as denoted by the vertical line  
468 representing the stimulus artefact). Each trace is an average of 8 waveforms.

469 Figure 4. Individual data for motor evoked potentials in tibialis anterior normalised to  
470 maximal muscle response during shortening and lengthening contractions at 15, 25, 50  
471 and 80% of contraction-type specific maximal torque.

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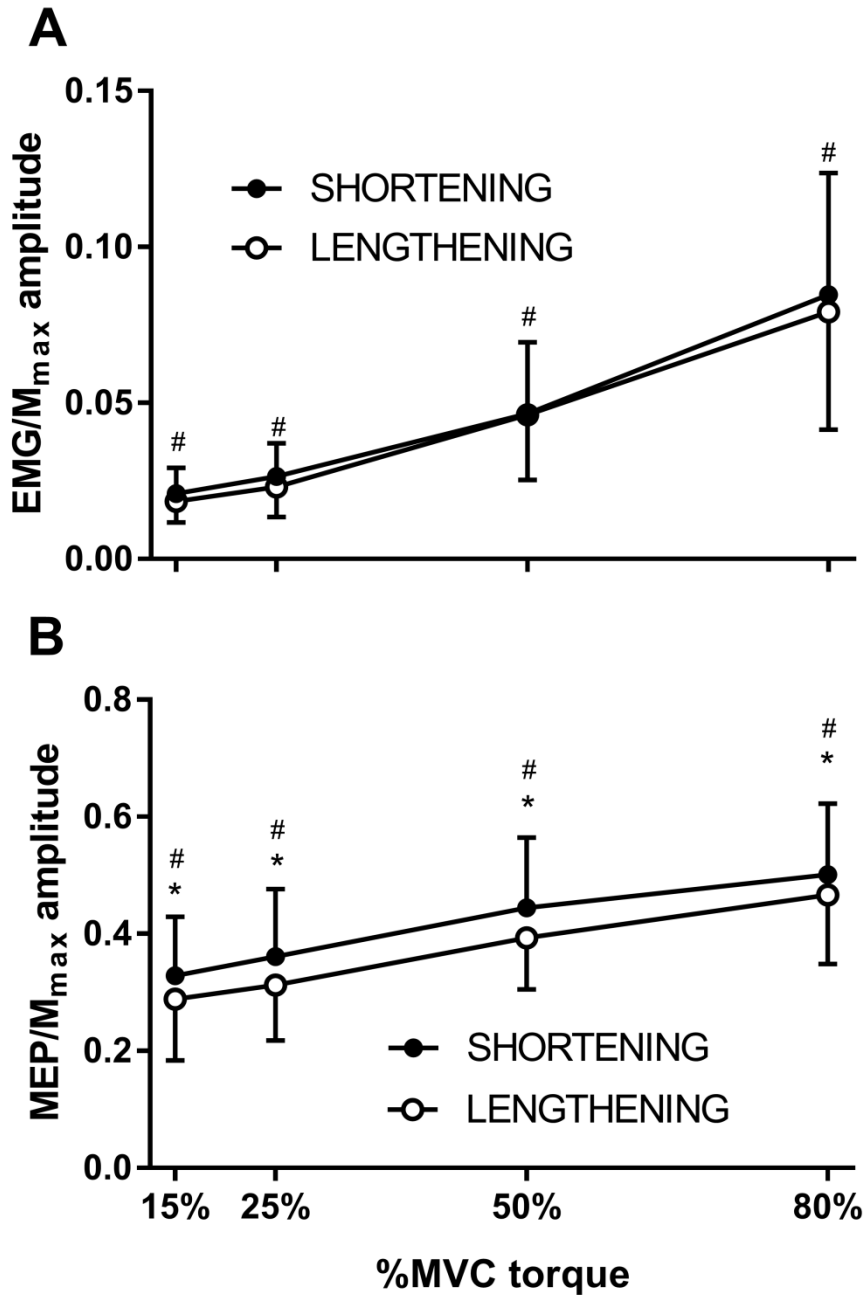
473 Figure 1



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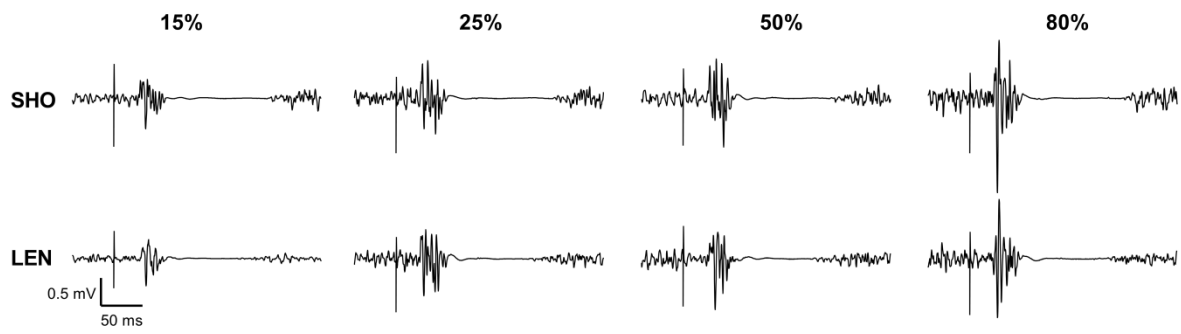




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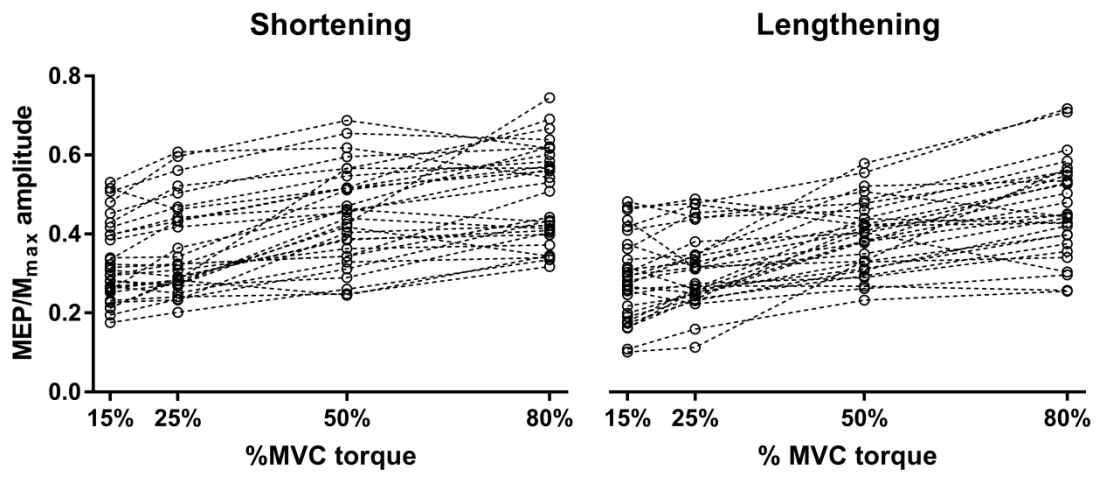
479 Figure 3



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481

482 Figure 4



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